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CERTIFICATE OF MAILING

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ELI LILLY AND COMPANY

By S R Reades Date 3-20-01



**PATENT APPLICATION**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | | |
|---|---|---|---|
| Applicant | : | Suad Efendic | |
| Serial No. | : | 09/400,802 | Group Art Unit: 1653 |
| Filed | : | September 22, 1999 | |
| For | : | Use of GLP-1 or analogs in Treatment of Stroke | Examiner F. Moezie |
| Docket No. | : | X-11158 | |

**Response to Restriction Requirement**

Assistant Commissioner for Patents
Washington, D.C. 20231
Sir:

Enclosed herewith is a petition for an extension of time under 37 C.F.R. § 1.136. The petition authorizes the office to charge the necessary fee under 37 C.F.R. § 1.17(a) to Deposit Account No. 05-0840 in the name of Eli Lilly & Co.

Claims 1-13 of this Application are currently pending. The Examiner has made a restriction requirement under 35 U.S.C. § 121. Applicants provisionally elect with traverse Group II and the species $Val^8$-GLP-1(7-37) [SEQ ID NO: 5]. Applicant is unclear how to elect an "ultimate specie." Neither the M.P.E.P. nor the Code of Federal Regulations addresses this requirement asserted by the Examiner. Further, there are numerous changes that can be made to native GLP-1 to generate analogs with activity. Applicants have described hundreds of these compounds in the Specification and all of these compounds have the common structural feature of the GLP-1 backbone. Applicants respectfully request that the

requirement for restriction be reconsidered primarily because the Examiner has improperly restricted out members of a Markush group.

The Examiner has indicated that because GLP-1 compounds, GLP-1 analogs, GLP-1 derivatives, compounds that act through the GLP-1 receptor, and compounds that enhance insulin sensitivity by acting through the GLP-1 receptor may be classified in different subclasses depending on the structure of the molecule, that the use of each of these compounds to treat stroke is a distinct invention.

Claim 1 encompasses the use of GLP-1, GLP-1 analogs, GLP-1 derivatives, and salts thereof to reduce the mortality and morbidity associated with stroke. These compounds are described extensively throughout the specification and share the common structural feature of the GLP-1 backbone. GLP-1 compounds which include analogs, derivatives, variants, precursors and homologues are discussed beginning on page 5, line 25. The sequence of native GLP-1(7-37) is provided at the bottom of page 5 and top of page 6. GLP-1 analogs are defined and exemplified on page 6, lines 3-12. Additional analogs which generally have one or two substitutions at various positions of native GLP-1(7-37) are described on page 6, line 26 through page 15. GLP-1 analogs that are resistant to DPP-IV cleavage are preferred and these analogs are discussed on page 12, lines 1-6. GLP-1 derivatives are defined and exemplified on page 6, lines 12-25. Additional derivatives are described on page 9 and pages 12 through 15.

These GLP-1 compounds are claimed as a Markush group. Applicant respectfully asserts that it is not proper to restrict out members of a Markush group especially when the compounds included within the group share a common utility and a substantial structural feature. *See* M.P.E.P. § 803.02. The compounds restricted out by the Examiner in this case share a common utility in that they have insulinotropic activity. They share common structural features of the native GLP-1 backbone, and they are all able to bind and activate a signal

through the GLP-1 receptor.

In distinguishing restriction requirements made between different claims and those made in the context of a Markush group, the Federal Circuit noted that "it is *never* proper for an examiner to reject a Markush claim under 35 U.S.C § 121. Section 121 simply does not authorize such a rejection." *In re Watkinson*, 900 F.2d 230, 232 (Fed. Cir. 1990). The M.P.E.P. § 803.02 points out two specific cases where the Board of Appeals reversed an Examiner's decision to restrict out claims of a Markush group. *See In re Weber*, 580 F.2d 455 (C.C.P.A. 1978); *In re Haas*, 580 F.2d 461 (C.C.P.A. 1978). In *Weber*, the court stated that "an applicant has a right to have Each claim examined on the merits" and noted that if a single claim is required to be divided up, that claim would never be considered on its merits. 580 F.2d at 458. The court held that while section 121 allows the restriction of independent and distinct inventions, "[i]t does not . . . provide a basis for an examiner acting under the authority of the Commissioner to Reject a particular Claim on that same basis." *Id.*

Thus, it is improper to restrict the method of using GLP-1 compounds, GLP-1 analogs, and GLP-1 derivatives to treat the mortality and morbidity associated with stroke into three groups. This requirement would prevent Applicants from ever having the claim as filed considered on the merits.

In conclusion, Applicants respectfully request reconsideration of the restriction requirement especially with respect to Groups I, II, and III. Restriction of the invention into Groups I, II, and III improperly restricts a Markush group. Further, Applicant respectfully notes that Applicant has received issued U.S. Patent No. 6,006,753 titled Use of GLP-1 or Analogs to Abolish Catabolic Changes after Surgery. Claim 1 of this issued patent provides:

> A method of attenuating post-surgical catabolic changes and insulin resistance, comprising, administering to a patient in need thereof a compound selected from the group consisting of GLP-1, GLP-1 analogs, GLP-1 derivatives, and pharmaceutically-acceptable salts

Please type a plus sign (+) inside this box → [+]

PTO/SB/17 (12/97)

Approved for use through 09/30/00. OMB 0651-0032

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

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# FEE TRANSMITTAL

Note: Effective November 1, 1999. Patent fees are subject to annual revision.

**TOTAL AMOUNT OF PAYMENT** ($)890.00

| Complete if Known | |
|---|---|
| Application Number | 09/400,802 |
| Filing Date | September 22, 1999 |
| First Named Inventor | Suad Efendic |
| Group Art Unit | 1653 |
| Examiner Name | F. Moezie |
| Attorney Docket Number | X-11158 |

## METHOD OF PAYMENT (check one)

1. [X] The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

Deposit Account Number: 05-0840

Deposit Account Name: Eli Lilly and Company

[X] Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17

[ ] Charge the Issue Fee Set in 37 CFR 1.18 at the Mailing of the Notice of Allowance

2. [ ] Payment Enclosed:

[ ] Check [ ] Money Order [ ] Other

## FEE CALCULATION

### 1. FILING FEE

| Large Fee Code | Entity Fee ($) | Small Fee Code | Entity Fee ($) | Fee Description | Fee Paid |
|---|---|---|---|---|---|
| 101 | 710 | 201 | 355 | Utility filing fee | |
| 106 | 320 | 206 | 160 | Design filing fee | |
| 107 | 490 | 207 | 245 | Plant filing fee | |
| 108 | 710 | 208 | 355 | Reissue filing fee | |
| 114 | 150 | 214 | 75 | Provisional filing fee | |

**SUBTOTAL (1)** ($)

### 2. CLAIMS

| | | Extra | | Fee from below | | Fee Paid |
|---|---|---|---|---|---|---|
| Total Claims | -20**= | | X | 18 | = | |
| Independent Claims | -3**= | | X | 80 | = | |
| Multiple Dependent Claims (first time) | | | | 270 | = | |

| Large Fee Code | Entity Fee ($) | Small Fee Code | Entity Fee ($) | Fee Description |
|---|---|---|---|---|
| 103 | 18 | 203 | 9 | Claims in excess of 20 |
| 102 | 80 | 202 | 39 | Independent claims in excess of 3 |
| 104 | 270 | 204 | 135 | Multiple dependent claim |
| 109 | 78 | 209 | 39 | Reissue independent claims over original patent |
| 110 | 18 | 210 | 9 | Reissue claims in excess of 20 and over original patent |

**SUBTOTAL (2)** ($)

**or number previously paid, if greater; For Reissues, see above

## FEE CALCULATION (continued)

### 3. ADDITIONAL FEES

| Large Fee Code | Entity Fee ($) | Small Fee Code | Entity Fee ($) | Fee Description | Fee Paid |
|---|---|---|---|---|---|
| 105 | 130 | 205 | 65 | Surcharge-late filing fee or oath | |
| 127 | 50 | 227 | 25 | Surcharge-late provisional filing fee or cover sheet. | |
| 139 | 130 | 139 | 130 | Non-English specification | |
| 147 | 2,520 | 147 | 2,520 | For filing a request for reexamination | |
| 112 | 920* | 112 | 920* | Requesting publication of SIR prior to Examiner action | |
| 113 | 1,840* | 113 | 1,840* | Requesting publication of SIR after Examiner action | |
| 115 | 110 | 215 | 55 | Extension for reply within first month | |
| 116 | 390 | 216 | 195 | Extension for reply within second month | |
| 117 | 890 | 217 | 445 | Extension for reply within third month | 890 |
| 118 | 1,390 | 218 | 695 | Extension for reply within fourth month | |
| 128 | 1,890 | 228 | 945 | Extension for reply within fifth month | |
| 119 | 310 | 219 | 155 | Notice of Appeal | |
| 120 | 310 | 220 | 155 | Filing a brief in support of an appeal | |
| 121 | 270 | 221 | 135 | Request for oral hearing | |
| 138 | 1,510 | 138 | 1,510 | Petition to institute a public use proceeding | |
| 140 | 110 | 240 | 55 | Petition to revive-unavoidable | |
| 141 | 1,240 | 241 | 620 | Petition to revive-unintentional | |
| 142 | 1,210 | 242 | 605 | Utility issue fee (or reissue) | |
| 143 | 430 | 243 | 215 | Design Issue Fee | |
| 144 | 580 | 244 | 290 | Plant Issue Fee | |
| 122 | 130 | 122 | 130 | Petitions to the Commissioner | |
| 123 | 50 | 123 | 50 | Petitions related to provisional applications | |
| 126 | 240 | 126 | 240 | Submission of Information Disclosure Stmt. | |
| 581 | 40 | 581 | 40 | Recording each patent assignment per property (times number of properties) | |
| 146 | 710 | 246 | 355 | Filing a submission after final rejection (37 CFR 1.129(a)) | |
| 149 | 710 | 249 | 355 | For each additional invention to be examined (37 CFR 1.129(b)) | |
| 179 | 710 | 279 | 355 | Request for Continued Examination (RCE) | |
| 169 | 900 | 169 | 900 | Request for expedited examination of a design application | |
| Other fee (specify) | | | | | |
| Other fee (specify) | | | | | |

*Reduced by Basic Filing Fee Paid

**SUBTOTAL (3)** ($)890.00

## SUBMITTED BY

| | | | |
|---|---|---|---|
| Typed Name | Mark J. Stewart, Ph.D. | Reg. Number | 43,936 |
| Signature | | Date | March 20, 2001 |

Complete (if applicable)

## CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231, on the date appearing below.

ELI LILLY AND COMPANY

By: _____ Date: 3-20-01

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